among seven erythrodermic patients who have been treated in the past 24 months with PUVA therapy, clearing of the condition has occurred in six. As observed with other types of mycosis fungoides, there was a recurrence of the disease in the four patients in whom treatment was not maintained. However, subsequent therapy controlled the disease and all the patients are being maintained on PUVA therapy indefinitely.

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## Skin Lesions in Bowel Bypass Syndrome

INTESTINAL BYPASS OPERATIONS as a treatment for morbid obesity have been used since the mid-1950's. Complications have included diarrhea, distention, abdominal pain, pneumatosis cystoides intestinalis, arthralgias, arthritis, renal calculi, gallstones, hepatic abnormalities, electrolyte disturbance and erythema nodosum-like skin eruptions. Three recent articles have reported papulopustular eruptions in six patients following bowel bypass operations.

Hansen and co-workers reported on two patients in whom arthritis, erythema nodosum, and a primarily acral erythematous eruption of papules and pustules developed following jejunoileal bypass operations. The arthritis was minimally responsive to nonsteroid antiinflammatory drugs. Both the arthritis and the skin eruptions improved on treatment with various antibiotic drugs including tetracycline, metronidazole, minocycline and erythromycin. One patient's condition relapsed when antibiotic treatment was withdrawn, but it was later controlled on therapeutic doses of zinc sulfate. Bowel symptomatology was absent. No serological evidence of circulating immune complexes was found. A biopsy specimen of skin from one patient showed an intraepidermal vesicle with a mild leukocytoclastic inflammation of dermal vessels. Direct immunofluorescence of skin was negative.

Goldman and co-workers reported on two patients with end-to-end jejunoileal bypass operations in whom arthralgia, arthritis and a primarily acral erythematous papular and pustular eruption developed. Bowel symptomatology was present in one patient and fever and chills in the other. The first patient responded initially to treatment with penicillin and tetracycline. Subsequently, she did not respond to antibiotic drugs, but did respond to aspirin; later her condition cleared spontaneously. The second patient's condition improved on carbenicillin therapy, while aspirin and nonsteroid antiinflammatory drugs were not helpful. Both patients had elevated erythrocyte sedimentation rates and negative complement 3 and 4 (C3 and C4). The first patient had negative findings on antinuclear antibodies (ANA), rheumatoid factor, cryoglobulin and platelet aggregation tests, but had HLA-B27 positive tissue typing and a positive complement consumption test. The second patient had a negative complement consumption test but a positive platelet aggregation test and ANA-positive 1:320 nucleolar pattern. Biopsy specimens of skin showed a leukocytoclastic vasculitis in both patients. Direct immunofluorescence of skin from the first patient was negative.

Dicken and colleagues reported on two patients who had a primarily acral and upper chest distribution of erythematous papules and pustules, and elevated temperatures following bowel bypass operations. The episodes lasted six days or less and tended to recur. Occasionally, myalgias and polyarthralgia were noted during episodes but not during quiescent periods. The first patient responded to administration of metronidazole. The second patient did not respond to ampicillin therapy but had some decrease in the frequency of eruptions with administration of tetracycline; clearing occurred after surgical restitution of the bypassed segment of bowel. A biopsy specimen of skin from the first patient showed a subepidermal vesicle with heavy mixed-cell dermal inflammation composed of lymphocytes, polymorphonuclear leukocytes and rare plasma cells. No evidence of vasculitis was reported. Direct immunofluorescence showed a patchy, weak basement membrane pattern with C3 but was negative for IgG, IgM and IgA.

The six patients exhibited a primarily acral and upper chest distribution of erythematous papules and pustules. The severity of polyarthralgia or arthritis seemed to parallel the course of the eruption and its response to antibiotic therapy. Serological evidence of circulating immune complexes was found in two of the six cases. Histological

evidence of vasculitis was present in three of four biopsy specimens.

Bacterial overgrowth in the bypassed bowel segments and immune complex formation in response to the excess of bacterial antigens have been suggested as the possible causes of extraintestinal manifestations of the bowel bypass syndrome. The response to antibiotic drugs, evidence of vasculitis in three cases and detection of immune complexes in two cases suggest that a similar pathogenesis may account for papulopustular eruptions seen in bowel bypass patients. However, present therapy is empirical and no single regimen has been consistently beneficial.

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## PUVA Carcinogenesis

THE EFFICACY OF PUVA treatment with orally given 8-methoxypsoralen (P) combined with long-wave ultraviolet radiation (UVA) for the clearing of severe psoriasis has been established. The palliative nature of this therapy is evidenced by the recurrence of psoriasis despite continued maintenance therapy once a week or less frequently. Treatment of recurrent psoriasis with PUVA on a more frequent schedule is a common procedure, which over the years may result in a large cumulative UVA irradiation dose expressed in terms of joules per cm.$^2$ The safe upper limit of ultraviolet A dosage from PUVA therapy is not known at this time.

The risk of carcinogenesis from chronic exposure to PUVA has been an early concern. In laboratory animals given large doses of psoralen topically or intraperitoneally plus UV light, a high incidence of squamous cell carcinomas and fibrosarcomas has occurred. The oral administration of psoralen in animals, once thought to be photoprotective, may also produce these tumors in conjunction with UV light. More and more evidence has emerged from in vitro studies that PUVA can be carcinogenic depending on the dose. PUVA has a mutagenic effect in bacterial systems. Sister chromatid exchanges, which have been employed as a cytologic means for the detection of potential carcinogens, have been observed in PUVA cells in vitro but not in vivo. It is known that exposure to nonionizing radiation and to PUVA can affect components of the immune system, which may play a role in photocarcinogenesis.

In humans, a type of epidermal dystrophic change similar to that which occurs in actinic keratoses has been observed in about half of 37 patients treated with PUVA. These changes, which were present at clearing and after a year of therapy, may indicate that cells have been altered genetically by somatic mutation. Whether the epidermal dystrophy is transient or represents a persistent abnormality is being investigated further.

Clinical evidence of PUVA carcinogenicity has emerged from a multicenter follow-up study of more than 1,300 patients. Stern and co-workers documented a total of 48 cases of basal cell and squamous cell carcinomas in 30 patients treated with PUVA during an average observation period of 2.1 years. A significant increase in the incidence of cutaneous cancer was found in patients with previous skin cancers and in those with a history of exposure to ionizing radiation, when compared with the expected risk for an age-sex and geographically-matched population. Of particular concern was an inverse in the expected ratio of basal cell epitheliomas to squamous cell carcinomas, as well as the frequent occurrence of squamous cell carcinomas in areas of the body that were not exposed to the sun. Whether all PUVA-treated patients will be at increased risk for cutaneous carcinogenesis after a longer period of latency has elapsed remains to be determined.

Because of a probable long latent period for carcinogenic effect, younger persons are at greater risk for long-term side effects. For this reason, the Committee on Drugs of the American Academy of Pediatrics has recommended that children not be enrolled in PUVA treatment programs.

A further concern relating to ocular damage following PUVA exposure is based on animal experiments. The exact length of time that photoactive psoralen remains in the lens of the eye is not known. Because of a risk of cataract formation, eyes must be carefully protected with UVA-blocking sunglasses from time of ingestion of psoralen throughout the active treatment program according to published guidelines. During treatment in the light unit, UVA-opaque goggles are worn.

PUVA therapy of psoriasis remains investigational. In selected patients with severe disabling